



FSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Guidance on the scientific requirements for health claims related to functions of the nervous system, including psychological functions.

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SCIENTIFIC OPINION

Guidance on the scientific requirements for health claims related to functions of the nervous system, including psychological functions¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2,3}

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

The European Food Safety Authority (EFSA) asked the Panel on Dietetic Products, Nutrition and Allergies to draft guidance on scientific requirements for health claims related to functions of the nervous system, including psychological functions. This guidance has been drawn from scientific opinions of the NDA Panel on such health claims. Thus, this guidance represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. It is not intended that the document will include an exhaustive list of beneficial effects and studies/outcome measures that are acceptable. Rather, it presents examples drawn from evaluations already carried out to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations. A draft of this guidance document was endorsed by the NDA Panel on 16 September 2011, and was released for public consultation from 17 October 2011 to 16 December 2011.

KEY WORDS

Health claims, scientific requirements, nervous system, psychological function.

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BACKGROUND AS PROVIDED BY EFSA

Regulation (EC) No 1924/2006⁴ harmonises the provisions that relate to nutrition and health claims and establishes rules governing the Community authorisation of health claims made on foods. According to the Regulation, health claims should be only authorised for use in the Community after a scientific assessment of the highest possible standard has been carried out by EFSA.

EFSA and its NDA Panel have been engaging in consultation with stakeholders and have published guidance on scientific substantiation of health claims since 2007⁵. Most recently, a briefing document on the scientific evaluation of health claims was published for consultation in April 2010, followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma, in June 2010⁶.

Based on experiences gained with the evaluation of health claims, and to further assist applicants in preparing and submitting their applications for the authorisation of health claims, the NDA Panel is asked to develop guidance documents on the scientific requirements for the substantiation of health claims in selected areas, in addition to the guidance for the scientific substantiation of health claims related to gut and immune function (EFSA-Q-2010-01139).

TERMS OF REFERENCE AS PROVIDED BY EFSA

The NDA Panel is requested by EFSA to develop guidance documents on the scientific requirements for health claims in the following areas:

- Post-prandial blood glucose responses/blood glucose control
- Weight management, energy intake and satiety
- Protection against oxidative damage
- Cardiovascular health
- Bone, joint and oral health
- Neurological and psychological functions
- Physical performance

Specific issues to be addressed in this guidance include:

- which claimed effects are considered to be beneficial physiological effects?
- which studies/outcome measures are appropriate for the substantiation of function claims and disease risk reduction claims?

Each guidance document should be subject to public consultation and may be followed up as appropriate by scientific meetings with experts in the field.

Before the adoption of each guidance document by the NDA Panel, the draft guidance shall be revised taking into account the comments received during the public consultation. A report on the outcome of the public consultation for each guidance document shall be published. All guidance documents should be finalised by July 2012.

⁴ Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

⁵ <http://www.efsa.europa.eu/en/nda/ndaclaims.htm>

⁶ <http://www.efsa.europa.eu/en/ndameetings/docs/nda100601-ax01.pdf>

ASSESSMENT

1. Introduction

To assist applicants in preparing and submitting their applications for the authorisation of health claims, EFSA and in particular its Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA) has ongoing consultations with stakeholders and has published guidance on scientific substantiation of health claims since 2007⁷. In April 2010, a draft briefing document on the scientific evaluation of health claims was published for consultation and was followed by a technical meeting with experts from the food industry, Member States and the European Commission in Parma, in June 2010. The draft briefing document has been transformed into a Panel output taking into account the questions/comments received. This document constitutes the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims and outlines the approach of the NDA Panel to the evaluation of health claims in general. In response to requests from industry, EFSA is engaged in further consultation with stakeholders and is developing additional guidance on specific types of claims.

The present guidance, prepared by the NDA Panel, on the scientific requirements for the substantiation of health claims related to functions of the nervous system, including psychological functions, was, prior to its finalisation, endorsed by the NDA Panel on 16 September 2011 for public consultation, which was open from 17 October 2011 to 16 December 2011. All the public comments received that related to the remit of EFSA were assessed, and the guidance has been revised taking into consideration relevant comments. The comments received and a report on the outcome of the public consultation have been published on the EFSA website.

The guidance document focuses on two key issues related to substantiation of health claims related to functions of the nervous system, including psychological functions:

- claimed effects which are considered to be beneficial physiological effects;
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

Issues which are related to substantiation that are common to health claims in general (e.g. characterisation of the food/constituent) are addressed in the general guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims⁸.

This document has been drawn from scientific opinions of the NDA Panel on health claims related to functions of the nervous system, including psychological functions. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas. The document should be read in conjunction with the briefing document for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims.

It is not intended that the document should include an exhaustive list of beneficial effects and studies/outcome measures which are acceptable. Rather, it presents examples drawn from evaluations already carried out to illustrate the approach of the Panel, as well as some examples which are currently under consideration within ongoing evaluations.

⁷ <http://www.efsa.europa.eu/en/nda/ndaclaims.htm>

⁸ EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.

2. General considerations

2.1. Beneficial physiological effect

According to Regulation (EC) No 1924/2006, the use of health claims shall only be permitted if the food/constituent, for which the claim is made, has been shown to have a beneficial physiological effect. For the purpose of this guidance document, physiological effects are broadly defined to encompass the nervous system, psychological, perceptual (i.e. related to sensory processes), psychomotor, and physiological regulatory effects. In assessing each claim, the NDA Panel makes a scientific judgement on whether the claimed effect is considered to be a beneficial physiological effect in the context of the specific claim as described in the information provided, taking into account the population group for whom the claim is intended. For function claims, a beneficial effect may relate to maintenance or improvement of a function.

For reduction of disease risk claims, 'beneficial' refers to whether the claimed effect relates to the reduction (or beneficial alteration) of a risk factor for the development of a human disease (not reduction of the risk of disease). A risk factor is a factor associated with the risk of a disease that may serve as a predictor of development of that disease. Whether or not the alteration of a factor is considered to be beneficial in the context of a reduction of disease risk claim depends on the extent to which it is established that:

- The factor is an independent predictor of disease risk (such a predictor may be established from intervention and/or observational studies);
- The relationship of the factor to the development of the disease is biologically plausible.

Except for well established risk factors, the extent to which the reduction of a factor is beneficial in the context of a reduction of disease risk claim needs to be considered on a case-by-case basis.

The NDA Panel considers that the population group for which health claims are intended is the general (healthy) population or specific subgroups thereof, for example elderly people, physically active subjects, and pregnant women. In its evaluation, the NDA Panel considers that where a health claim relates to a function/effect that may be associated with a disease, subjects with the disease are not the target population for the claim, for example Alzheimer disease patients. Applications for claims that specify target groups other than the general (healthy) population are the subject of ongoing discussions with the Commission and Member States with regard to their admissibility.

The NDA Panel also considers whether the claimed effect is sufficiently defined to establish that the studies identified for substantiation of the claim were performed with (an) appropriate outcome measure(s) of that claimed effect. Reference to general, non-specific benefits of the nutrient or food for overall good health or health-related well-being may only be made if accompanied by a specific health claim.

2.2. Studies/outcome measures appropriate for substantiation of claims

As human studies are central for substantiation of health claims, the document focuses in particular on such studies. In considering whether the studies provided are pertinent (i.e. studies from which conclusions can be drawn for the scientific substantiation of the claim), the NDA Panel addresses a number of questions, including:

- Whether the studies have been carried out with the food/constituent for which the claim is made. This requirement means that there should be sufficient definition of the food/constituent for which the claim is made, and of the food/constituent that has been investigated in the studies that have been provided for substantiation of the claim. The evaluation also considers

how the conditions under which the human studies were performed relate to the conditions of use (e.g. quantity and pattern of consumption of the food/constituent) proposed for the claim.

- Whether the design and quality of the studies allow conclusions to be drawn for the scientific substantiation of the claim. The evaluation takes into account the hierarchy of evidence as described in the scientific and technical guidance of the NDA Panel⁹, for example intervention studies generally provide stronger evidence than observational studies. Intervention studies should be appropriately conducted so as to minimise bias. In observational studies adequate control of confounders is important. Each health claim is assessed separately and there is no pre-established formula as to how many or what type of studies are needed to substantiate a claim. In this regard, the reproducibility of the effect of the food/constituent as indicated by consistency between studies is an important consideration.
- Whether the studies have been carried out in a study group representative of the population group for which the claim is intended. Can the results obtained in the studied population be extrapolated to the target population? For studies in groups (e.g. subjects with a disease) other than the target group (e.g. general population) for a claim, the NDA Panel considers on a case-by-case basis the extent to which it is established that extrapolation from the study group to the target group is biologically plausible.
- Whether the studies used (an) appropriate outcome measure(s) of the claimed effect. For this, the NDA Panel considers what is generally accepted in the relevant research fields (e.g. guidelines published by scientific societies based on rigorous methodological approaches), and consults experts from various disciplines, as appropriate.

3. General claims on functions and development of the nervous system

Improvement, maintenance or reduced loss of the functions of the nervous system is generally considered a beneficial physiological effect.

General claims on the maintenance of (unspecified) functions of the nervous system have been proposed for some essential nutrients. The scientific substantiation of these claims was based on the well-established biochemical role of such nutrients in neural transmission, or on deficiency symptoms involving the nervous system.

For non-essential food constituents, claims on the improvement, maintenance or reduced loss of (unspecified) neural, brain or psychological functions in general are not sufficiently defined for a scientific evaluation. The specific function of the nervous system which is the subject of the claim, together with appropriate outcome measures which may be used for the scientific evaluation of the claimed effect *in vivo* in humans, must be identified. Claims on specific functions of the nervous system are discussed in Section 4 of this document.

Also contribution to the normal development of the nervous system is considered a beneficial physiological effect. Claims on the normal development of the nervous system (including brain development) have been proposed for infants and children in relation to some essential nutrients. The scientific substantiation of these claims was based on deficiency symptoms involving the nervous system in these population subgroups. For non-essential food constituents, claims on the normal development of the nervous system, including brain development, are not sufficiently defined for a scientific evaluation. The specific aspect of the development of the nervous system which is the subject of the claim (e.g. specific aspects of cognitive development and visual development), and the

⁹ EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. Scientific and technical guidance for the preparation and presentation of an application for authorisation of a health claim (revision 1). EFSA Journal, 9(5):2170, 36 pp.

particular life stage to which the claim applies, should be specified. Claims related to cognitive and visual development are discussed in Sections 4.1 and 4.3 of this document, respectively.

4. Claims on specific functions of the nervous system

4.1. Claims on cognitive function

Cognitive function encompasses several domains, including memory, attention (concentration), alertness, learning, intelligence, language, and problem solving, which are well defined psychological constructs. An increase, maintenance or reduced loss of cognitive function in one or more of its domains is a beneficial physiological effect.

The scientific evidence for the substantiation of health claims related to one or more specific domains of cognitive function can be obtained from human intervention studies showing an effect on objective measures of the specific domain(s) by using standard psychometric tests (e.g. standard 'computerised' or 'paper-and-pencil' tests), established test batteries, or valid and reliable tests for the specific domain(s) that is/are the subject of the claim (see Sections 4.1.3 to 4.1.5). Claims may refer to acute effects (i.e. temporary effects occurring shortly after consumption of the food/constituent) or to longer-term effects (i.e. measurable in fasting conditions with repeated consumption of the food/constituent). Acute effects should be demonstrated during repeated consumption of the food/constituent in order to exclude adaptation through compensatory mechanisms. Evidence for an effect on the incidence of clinically diagnosed cognitive diseases (e.g. dementia) by using valid clinical diagnostic tools could also be used for the scientific substantiation of a claim on the maintenance of cognitive function.

Evidence that the psychometric tests or test batteries used for the objective assessment of cognitive endpoints are appropriate for the study population should be provided. When a study involves the repeated use of cognitive tests, the possible confounding effect of practice needs to be addressed. Practice effects should be considered in the study design and/or addressed by using adequate statistical methods. Appropriate methods to address practice effects depend on the context of the study, and should be selected and justified on a case-by-case basis. The consistency of the effects observed, and the repeatability of the results, are important considerations when reviewing the evidence.

Measures of the neural activity of the brain (e.g. event-related potentials (ERPs) and functional magnetic resonance imaging) obtained during the performance of a relevant cognitive task may be used as supportive evidence for the psychometric assessment of cognitive endpoints for the scientific substantiation of health claims on cognitive function.

With respect to the study population, results from studies conducted in subjects with mild cognitive decline, without clinical diagnosis of dementia or other psychological or neurological diseases which may be responsible for the impairment, could be used for the scientific substantiation of claims on cognitive function, as long as the methods and inclusion/exclusion criteria used to characterise the study group are clearly defined. The rationale for extrapolation of the results obtained in patients with clinical diagnosis of a cognitive disease (e.g. dementia) to the target population for the claim (e.g. subjects without the disease) should be provided, and will be considered on a case-by-case basis (e.g. evidence that the mechanism by which the food constituent may exert the claimed effect on cognition in subjects with the disease is also relevant for subjects without the disease). Where appropriate, the confounding role of medication should be considered (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

Contribution to the development of one or more specific domains of cognitive function is also considered to be a beneficial physiological effect for infants and small children. Cognitive development relates to the maturation and progression of cognitive abilities over time. The particular life stage to which the claim applies should be specified. The scientific evidence for the substantiation

of health claims related to the development of one or more specific domains of cognitive function can be obtained from human intervention studies showing an effect on valid neurodevelopmental tests designed to assess the specific domain(s) which is/are the subject of the claim in the age range of the study group. Consistency of results between different tests within and between studies is an important consideration, and will be evaluated on a case-by-case basis.

4.1.1. Claims on alertness

Alertness, defined as a cognitive construct, refers to a state of enhanced arousal and readiness to receive and process information, and to respond. Maintenance (i.e. reduced loss) of cognitive alertness is a beneficial physiological effect for subjects wishing to improve their level of alertness. Changes in cognitive alertness can be measured using valid psychometric tests, which determine reaction time or speed of response to standardised tasks (e.g. measures of reaction time in simple reaction time tests, choice reaction time tests or standard vigilance tests measuring speed of reactions).

The term, 'alertness', may also relate to a specific mood/affect construct (i.e. 'feeling alert'). An improvement in alertness as a mood/affect construct (e.g. assessed by self-rating scales) is not necessarily associated with an increased performance in reaction time or speed of response. Therefore, self-rating scales of alertness cannot be used to substantiate a claim on cognitive alertness.

4.1.2. Claims on attention

Attention (concentration), defined as a cognitive construct, refers to the ability to attend to, select and use incoming sensory information. There are two broad categories of attention. Selective attention is the ability to concentrate on one task or source of information to the exclusion of others. Sustained attention (vigilance) is the ability to concentrate over a period of time. The increase, maintenance or reduced loss of selective attention, sustained attention, or both, is considered to be a beneficial physiological effect.

Various valid psychometric tests can be used to assess changes in either selective attention (e.g. visual selective search tests, and categorical search attention tests) or sustained attention (e.g. continuous performance tasks, rapid visual information processing tasks, and visual or auditory vigilance tasks), whereas standardised attention test batteries allow a comprehensive assessment of the full spectrum of attention by using sets of tests. Accuracy and reaction time/speed of response measures should be considered together in order to assess performance of attention tests and control for speed-accuracy trade-off.

With respect to the study population, results from studies conducted in subjects with impaired attention without clinical diagnosis of attention deficit disorders (e.g. attention deficit hyperactivity disorders, ADHD) or other psychological or neurological diseases which may be responsible for the impairment could be used for the scientific substantiation of claims on attention, as long as the methods and inclusion/exclusion criteria used to characterise the study group are clearly defined. The rationale for extrapolation of the results obtained in subjects with clinical diagnosis of attention disorders (e.g. ADHD) to the target population (e.g. subjects without the disease) should be provided, and will be considered on a case-by-case basis (e.g. evidence that the mechanism by which the food constituent may exert the claimed effect on attention in subjects with the disease is also relevant for subjects without the disease). Where appropriate, the confounding role of medication should be considered (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

4.1.3. Claims on memory

Memory is the cognitive ability to maintain previously learned information, so that it may be accessed and used at a later time. Memory is not a unitary construct but instead reflects a number of distinct cognitive processes (e.g. working memory, explicit memory and implicit memory). The improvement, maintenance or reduced loss of one or more cognitive processes related to memory is considered to be a beneficial physiological effect.

Changes in different aspects of memory (e.g. working memory, explicit memory and implicit memory) can be measured using valid psychometric tests.

4.2. Claims on mood/affect

Affect encompasses defined states or traits such as positive (characterised by, for example, enthusiasm and calmness) or negative (characterised by, for example, confusion, feeling depressed, fatigue, tension and anxiety) mood. Enhancement of mood/affect (i.e. the increase, maintenance or reduced loss of one or more positive affect traits; the decrease in one or more negative affect traits) is a beneficial physiological effect for subjects wishing to improve their mood.

The scientific evidence for the substantiation of health claims related to the enhancement of mood/affect in one or more of its traits can be obtained from human intervention studies showing an effect on self-reported measures of the specific trait(s) by using comprehensive assessment tools (e.g. comprehensive self-rating adjective checklists or visual analogue mood scales) and/or specific, valid and reliable tests for the particular trait(s) of mood/affect which is (are) the subject of the claim. Evidence for a sustained effect with repeated consumption of the food/constituent should be provided. Evidence for an effect on the incidence of clinically diagnosed depression by using valid clinical diagnostic tools could also be used for the scientific substantiation of a claim on the enhancement of mood.

Evidence that the comprehensive or specific psychometric tests used for the subjective assessment of mood/affect endpoints are appropriate for the study population should be provided. When experimental mood-induction techniques are used in human intervention studies, evidence/a rationale for the validity of such experimental models should also be provided, and will be considered on a case-by-case basis as supportive evidence for the scientific substantiation of these claims.

With respect to the study population, the rationale for extrapolation of results obtained in patients with a clinically diagnosed affective disorder (e.g. depression) to the target population for the claim (e.g. subjects without the disorder) should be provided, and will be considered on a case-by-case basis (e.g. evidence on whether the mechanism by which the food constituent may exert the claimed effect on enhancement of mood in subjects with the disease is also relevant for subjects without the disease). Where appropriate, the confounding role of medication should be considered (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

4.2.1. Claims on psychological stress

In the psychological domain, “stress” is a defined subjective construct which refers to a particular emotional state characterised by psychological distress or tension, resulting from external stressors. Alleviation of psychological stress is a beneficial physiological effect.

The scientific evidence for the substantiation of health claims related to psychological stress can be obtained from human intervention studies showing an effect on self-reported measures of psychological stress by using standard psychometric tools, which include valid visual analogue scales, self-reported scales or questionnaires, and clinician/observer scales.

Anxiety may be only one of the features of the affective responses to psychological stress. Therefore, measures of anxiety could be considered among appropriate endpoints for a claim on psychological stress, but they are not sufficient on their own.

There is no established specific biomarker of psychological stress. Concomitant changes in biological parameters associated with acute responses to psychological stress (e.g. blood concentrations of cortisol, heart rate, salivary IgA or other appropriate markers) could be used as supportive evidence for the subjective assessment.

With respect to the study population, results from studies conducted in “stress vulnerable/sensitive” subjects without a clinically diagnosed psychological disease could be used for the scientific substantiation of claims on psychological stress, as long as the methods and inclusion/exclusion criteria used to characterise the study group are clearly defined. For the purpose of characterising the study group, validated scales or questionnaires, together with appropriate normal values and cut-off scores, may be used. The rationale for extrapolation of the results obtained in patients with a clinically diagnosed psychological disease to the target population (e.g. subjects without the disease) should be provided, and will be considered on a case-by-case basis (e.g., evidence that the mechanism by which the food constituent may exert the claimed effect on attention in subjects with the disease is also relevant for subjects without the disease). Where appropriate, the confounding role of medication should be considered (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

4.2.2. Claims on anxiety

Anxiety is an affective state characterised by the apprehensive anticipation of perceived danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension. A reduction of anxiety is a beneficial physiological effect.

The scientific evidence for the substantiation of health claims related to anxiety can be obtained from human intervention studies showing an effect on self-reported measures of anxiety by using standard psychometric tools, which include valid visual analogue scales, self-reported scales or questionnaires, and clinician/observer scales. Evidence for an effect on the incidence of clinically diagnosed anxiety disorders by using valid clinical diagnostic tools could also be used for the scientific substantiation of a claim on the reduction of anxiety.

With respect to the study population, the considerations made for claims on psychological stress apply.

4.3. Claims on vision

Vision is a defined function of the eye and nervous system. An increase, maintenance or reduced loss of vision is a beneficial physiological effect for the general population, including, for example, visual display terminal workers. Claims may focus on vision under specific light conditions, for example, improvement of visual adaptation to the dark.

The scientific evidence for the substantiation of health claims related to vision can be obtained from human intervention studies showing an effect on visual function by using standard tests of visual acuity and contrast sensitivity (e.g. measures of contrast acuity thresholds, and distance and near-visual acuity tests). Evidence for an effect on the incidence of clinically diagnosed eye-related diseases associated with the impairment of vision (e.g. age-related macular degeneration, and cataract) by using valid clinical diagnostic tools could also be used for the scientific substantiation of claims on the maintenance of vision.

Changes in macular pigment optical density (MPOD) have been proposed as outcome measures for the scientific substantiation of claims on the maintenance of vision. However, MPOD is not a measure of visual function, and the available evidence does not establish that changes in macular pigment density predict changes in visual function. Therefore, MPOD is not a suitable outcome measure for the scientific substantiation of claims related to the maintenance of vision.

The available evidence does not establish that changes in MPOD predict the risk of eye-related diseases associated with vision impairment (e.g. age-related macular degeneration). Therefore, changes in MPOD may be considered as a risk factor for eye-related diseases associated with vision impairment only if changes in MPOD are accompanied by evidence of reduced incidence of these diseases in humans in the context of a particular nutritional intervention.

With respect to the study population, subjects with vision deficits without clinically diagnosed diseases which may be responsible for the deficit could be an appropriate study group for claims on the maintenance of vision, as long as the methods and inclusion/exclusion criteria used to characterise the study group are clearly identified in the study design. The rationale for extrapolation of the results obtained in patients with a clinically diagnosed impairment of vision (e.g. cataract, age-related macular degeneration, diabetic retinopathy, inherited retinal degeneration, and retinal vascular occlusive disease) to the target population for the claim (e.g. subjects without the vision impairment) should be provided, and will be considered on a case-by-case basis (e.g. evidence that the mechanism by which the food constituent may exert the claimed effect in patients with the disease is also relevant for subjects without the disease). Where appropriate, the confounding role of medication should be considered (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

Contribution to the visual development of infants and small children is also considered to be a beneficial physiological effect. The particular life stage to which the claim applies should be specified. Visual development, i.e. retinal and visual pathway maturation, can be estimated by objective methods, such as visual evoked potential (VEP) acuity testing (e.g. sweep VEP acuity), electroretinogram (ERG), and subjective standardised behavioural measures of visual acuity (e.g. acuity cards).

4.4. Claims on sleep

Specific aspects of sleep include sleep onset latency (time taken to fall asleep), sleep duration, sleep efficiency (ratio of total sleep time to total time in bed), and sleep quality (defined as perceived quality of sleep). Maintenance or improvement of one or more aspects of sleep is a beneficial physiological effect.

The scientific evidence for the substantiation of health claims related to one or more aspects of sleep can be obtained from human intervention studies showing an effect on subjective or objective measures of sleep by using valid scales and questionnaires (e.g. global symptom questionnaire or index), sleep diaries, polysomnography or actigraphy. Questionnaires which assess quality of life are not specific measures of sleep, and cannot be used on their own for the scientific substantiation of claims on sleep.

For claims on sleep quality, which is defined as perceived quality of sleep, an effect on valid subjective methods for assessing perception of sleep quality (e.g. valid self-rating scales and questionnaires) is required. Objective measures of sleep characteristics could be used as supportive evidence for the subjective assessment.

With respect to the study population, subjects with sleep disturbances without clinically diagnosed sleep disorders or other psychological or neurological diseases which may be responsible for the impairment could be an appropriate study group for claims on sleep, as long as the methods and

inclusion/exclusion criteria used to characterise the study group are clearly identified in the study design. The rationale for extrapolation of results obtained in patients with clinically diagnosed sleep disorders to the target population for the claim (e.g. subjects without the disorders) should be provided, and will be considered on a case-by-case basis (e.g. evidence on whether the mechanism by which the food constituent may exert the claimed effect in patients with sleep disorders is also relevant for subjects without the disorder). Where appropriate, the confounding role of medication should be considered (e.g. evidence for a lack of interaction between the food and the medications used on the claimed effect).

CONCLUSIONS

The guidance document focuses on two key issues regarding the substantiation of health claims related to functions of the nervous system, including psychological functions:

- claimed effects which are considered to be beneficial physiological effects;
- studies/outcome measures which are considered to be appropriate for the substantiation of health claims.

The document has been drawn from scientific opinions of the NDA Panel on health claims related to functions of the nervous system, including psychological functions. Thus, it represents the views of the NDA Panel based on the experience gained to date with the evaluation of health claims in these areas.

GLOSSARY AND ABBREVIATIONS

ADHD	Attention deficit hyperactivity disorders
ERG	Electroretinogram
ERP	Event-related potential
IgA	Immunoglobulin A
MPOD	Macular pigment optical density
VEP	Visual evoked potential